UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,154	01/19/2001	Clive Patience	61750-311	1279

7590 07/17/2002

Allen J. Grant, Esq.,
c/o Carella, Byrne, Bain, Gilfillan,
Cecchi, Stewart & Olstein
6 Becker Farm Road
Roseland, NJ 07068

EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	8

DATE MAILED: 07/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/766,154	Applicant(s) PATIENCE, CLIVE	
	Examiner Anne M Wehbé	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response to the restriction/election received on 4/25/02 has been entered. Applicant's election with traverse of the subject matter of Group III, claims 26-44, is acknowledged. Claims 1-44 are pending in the instant application. Of these, claims 1-25 are withdrawn as being drawn to subject matter non-elected with traverse in paper no.7. Claims 26-44 are currently under examination. An action on the merits follows.

Election/Restriction

Applicant's election with traverse of group III, claims 26-44 in Paper No.7 is acknowledged. The traversal is on the ground(s) that the in vitro screening methods recited in the claims of invention II can be used in the methods of selective breeding of invention III. This is not found persuasive because the methods of selective breeding of invention III do not require the use of the in vitro screening process of invention II and in that the screening process of invention II can be used for other purposes than for the process of selective breeding of invention III, such as for testing the cells of transplant recipients for ERV transmission. Thus, for the reasons discussed above and in the previous office action, the restriction requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification discloses methods for producing a human-tropic ERV-free animal comprising mating male and female animals from the same species wherein at least one of the animals is positive fro a human-tropic ERV-locus, and selecting for offspring free of human-tropic ERV.

The specification does not provide a sufficient written description for the scope of ERV and the scope of animals encompassed by the instant claims. The specification is primarily directed to the selective breeding of pigs, and in particular miniature pigs, in order to produce a pig which is free of at least one porcine endogenous retrovirus (PERV) capable of infecting human cells. The specification fails to provide any description of any human tropic ERV which is not a PERV. The specification discloses that most mammals contain numerous copies of endogenous retroviruses (ERV). However, the specification does not provide any guidance as to the identity

or the physical, structural, or biological characteristic of any other ERV than PERV. Furthermore, while the specification provides both description and evidence of PERV which are capable of infecting human cells, the specification provides no description of any non-PERV endogenous retrovirus which is infectious for human cells. In addition, the claims as written read on a process of mating any type of animal which is positive for a human-tropic ERV-locus. Aside from swine, the specification provides no description of any animal species which naturally contains human-tropic ERV.

The specification also fails to provide sufficient description for ERV loci or oligonucleotide primers or probes capable of detecting human-tropic ERV loci other than type-c PERV loci. The specification provides no guidance as to the sequences of any ERV which is not a PERV, or provide any description of oligonucleotides which are capable of recognizing and binding ERV loci from any and all species of animals. Thus, in the absence of any specific teachings in the specification concerning the identity, sequence, structural or physical characteristic of any ERV other than type C PERV, and in the absence of any description of non-PERVs which are human-tropic, the specification fails to meet the requirements for written description under 35 U.S.C. 112, first paragraph.

The applicant is reminded that *Vas-Cath Inc. v. Mahurkar,* 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is claimed." (See page 1117). The specification does

not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Adequate written description requires more than a mere statement that it is part of the invention. Based on the applicant's specification, the skilled artisan cannot envision the detailed chemical structure of human-tropic ERV loci, or envision the primer sequences and probes capable of detecting human-tropic ERV loci in cells in vivo or in vitro, therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel,* 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016. Please note as well that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

Claims 28-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process of producing a human-tropic PERV free pig from parental pigs wherein at least one parental pig is human-tropic PERV positive comprising: a) determining the number of human-tropic PERV in a male pig and a female pig, b) mating a male and a female pig wherein the male and female pigs are positive for at least one PERV locus and negative for different PERV-loci thereby producing offspring, c) selecting offspring which are free of at least one human tropic PERV loci, and d) repeating step a) with the offspring of step c), and e) selecting the offspring of step d) which are free of human tropic PERV, does not reasonably provide enablement for processes of producing any animal which is free of any type of human-

tropic ERV. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification is primarily directed to the selective breeding of pigs, and in particular miniature pigs, in order to produce a pig which is free of at least one and preferably all porcine endogenous retrovirus (PERV) capable of infecting human cells. The specification's working examples are limited to the detection of PERV loci present in highly inbred pig lines which are capable of infecting human cells. The specification's working examples demonstrate that while the A/A and C/C haplotype inbred pigs contain PERV which are capable of infecting human cells in vitro, the D/D/ haplotype inbred pigs appear to lack PERV which are capable of infecting human cells. In addition, the working examples demonstrate the use of PERV specific primers for screening cells infected with or carrying specific PERV loci. Finally, the working examples provide a prophetic breeding strategy for mating pigs carrying known PERV loci in order to obtain pigs which lack PERV loci infectious for humans.

As discussed in detail above, the specification fails to provide sufficient guidance as to animals other than pigs which contain human-tropic endogenous retroviruses. The specification also fails to provide sufficient guidance as to the characteristics, properties, and most importantly sequences of ERV loci other than type c PERV which are naturally or artificially present in any animal species. In particular, the specification fails to provide sufficient guidance as to primer sequences useful for detecting particular ERV loci in offspring of mated ERV positive animals

such that offspring which are ERV negative can be selected. Since endogenous retroviruses are not expressed in their native species under normal physiological conditions and have not been reported in the literature to result in any observable phenotype, detection and selection of animals which do nor do not contain particular ERVs requires detection of the ERV loci itself. Neither the specification nor the art at the time of filing provides any guidance as to methods of detecting a particular non-expressed genetic sequence in an animal which does not utilize sequence specific detection methods using oligonucleotide primers or probes. Thus, in order to select candidate animals for mating, and to select offspring which are positive or negative for human-tropic ERV, sequence information for human-tropic ERV loci necessary for primer or probe construction is required. In the absence of such information, the skilled artisan would not have been able to determine which animals to mate in order to produce an offspring which is free of human-tropic ERV. As such, it would have required undue experimentation for the skilled artisan at the time of filing to selectively breed any species of animal so as to produce an animal free of human-tropic ERV.

The applicant is also reminded that case law states that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. In re Goodman, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing In re Vaeck, 20 USPQ2d at 1445 (Fed. Cir. 1991). Furthermore, the Federal Circuit has stated that:

> a specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a

> rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, **when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art**. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1005 (CAFC 1997) (emphasis added).

Thus, by failing to disclosure the identity, properties, sequences and characteristics of endogenous retroviruses other than the type C porcine endogenous retroviruses, and further by failing to identify animals other than pigs which naturally carry human-tropic ERV, the specification fails to meet the enablement requirement for how to make and use the invention as claimed. Therefore, based on the lack of guidance present in the specification for non-PERV retroviruses, and for animals other than pigs which carry human-tropic ERV, it would have required undue experimentation to practice the scope of the claims as written.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites in step (a), " .. wherein at least of said animals....". The claim as

written is confusing and appears to be missing a word after "least". Amendment of the claim to correct this error is suggested in order to overcome this rejection.

Claims 39-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recites pigs carrying combinations of PERV 1, 2, 3, or 4. The literature both before and after the time of filing does not teach PERV which are labeled PERV 1 or PERV 2 etc. It appears from the applicant's disclosure that these numbers are arbitrary numbers and do not relate to any specific PERV or pigs carrying any particular PERV or combination or PERVs. Thus, the designation of PERV as PERV 1, 2, 3, or 4 is indefinite as the metes and bounds of the PERV or pigs carrying PERV cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaeffer et al. (1976) Transplantation, Vol. 22, 559-567. The applicant claims inbred miniature swine of DD haplotype which are inbred so as to remove infectious PERV gene sequences from the genome thereof.

Kaeffer et al. teaches miniature DD haplotype swine (Sachs et al., page). Please note that the applicant states in their specification that the miniature DD haplotype swine does not naturally contain infectious PERV. Thus, the lack of infectious PERV is an inherent property of the miniature DD haplotype swine. Further, "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). Thus, by teaching all the elements of the claims as written, Kaeffer et al. anticipates the instant invention.

The applicant is reminded that the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993), In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ2d 1922, 1923 (BPAI 1989).

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé